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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,103	07/05/2002	Sandrine Lentsch Graf	01-1081	4719
20306	7590	06/03/2004	EXAMINER	
MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP 300 S. WACKER DRIVE 32ND FLOOR CHICAGO, IL 60606			FORD, VANESSA L	
			ART UNIT	PAPER NUMBER
			1645	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/937,103

Applicant(s)

GRAF ET AL.

Examiner

Vanessa L. Ford

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 12 March 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **FINAL ACTION**

1. This Office Action is responsive to Applicant's amendment and response filed March 12, 2004. Claims 1-2 and 9-10 have been amended. Claims 11-16 have been added.

### ***Rejections Withdrawn***

2. In view of Applicant's amendment and response the following Objections and Rejections have been withdrawn:

- a) Objection to the claims, page 2, paragraph 1 of previous Office action.
- b) Objection to the specification, page 2, paragraph 3 of previous Office action.
- c) Objection to the claims, page 2, paragraph 3, of previous Office action.
- d) Objection to the claim 9, page 2, paragraph 4, of previous Office action.
- e) Rejection of claims 9-10 under 35 U.S.C. 112, second paragraph, page 3, paragraph 5 of previous Office action.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

### ***Rejections Maintained***

4. The rejection of claims 1-4 under 35 U.S.C. 102(e) is maintained for the reasons set forth on pages 4-5, paragraph 6 of the previous Office Action.

The rejection is on the grounds that LaPosta et al teach a liquid vaccine composition comprising a polysaccharide covalently bound to a protein (column 4, lines 60-65). LaPosta et al teach that sugars such as trehalose may be added to the vaccine composition to prevent aggregation (i.e. stabilize) of the vaccine composition (column 3, lines 10-26). LaPosta et al anticipate the claimed invention. LaPosta et al teach suitable antigens used in the vaccine include antigens from *Haemophilus influenzae*, *Neisseria meningitidis* and *Streptococcus pneumoniae*, Group A *Streptococcus* and

Art Unit: 1645

Group B *Streptococcus* (column 4, lines 25-64). LaPosta et al teach that the antigens of the invention, for example, bacterial capsular polysaccharide or a fragment thereof is chemically linked to a protein carrier molecule in order to enhance immunogenicity (column 4, lines 60-64). LaPosta, et al anticipates the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's vaccine and the vaccine of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the vaccine does not possess the same material structural and functional characteristics of the claimed vaccine). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant urges that LaPosta et al do not anticipate the claimed invention.

Applicant urges that LaPosta et al is focused on solving the problem of settling out and aggregation in prior art lyophilized compositions. Applicant urges that nowhere do

LaPosta et al specifically disclose the particular combination of an antigen consisting of trehalose and a polysaccharide bound to a carrier protein.

Applicant's arguments filed March 12, 2004 have been fully considered but they are not persuasive. LaPosta et al teach a liquid vaccine composition comprising a polysaccharide covalently bound to a protein. LaPosta et al teach that antigen that may be included in the vaccine composition include antigens from *Haemophilus influenzae*, *Neisseria meningitidis* and *Streptococcus pneumoniae*. LaPosta et al teach that sugars such as trehalose may be added to the vaccine composition to prevent aggregation (i.e. stabilize) of the vaccine composition. Applicant has provided no side-by-side composition to show that the claimed vaccine compositions differ from that of the prior art. Therefore, it is the Examiner's position that the vaccine compositions as taught by LaPosta et al anticipate the claimed invention.

5. The rejection of claims 9-10 under 35 U.S.C. 102/103 is maintained for the reasons set forth on pages 5-6, paragraph 7 of the previous Office Action.

The rejection was on the grounds that LaPosta et al teach a method of stabilizing a liquid vaccine composition comprising at least one antigen consisting of a polysaccharide bound to a carrier protein, wherein it consists in adding trehalose to the vaccine composition by teaching that sugars such as trehalose may be added to the vaccine composition to prevent aggregation (i.e. stabilize) of the vaccine composition (column 3, lines 10-26). LaPosta et al teach suitable antigens used in the vaccine include antigens from *Haemophilus influenzae*, *Neisseria meningitidis* and *Streptococcus pneumoniae*, Group A *Streptococcus* and Group B *Streptococcus* (column 4, lines 25-64). LaPosta et al teach that the antigens of the invention, for example, bacterial capsular polysaccharide or a fragment thereof is chemically linked to a protein carrier molecule in order to enhance immunogenicity (column 4, lines 60-64). The method of LaPosta et al is the same as the claimed method. LaPosta et al do not specifically teach the claimed quantities of trehalose added to the vaccine compositions. However, in the alternative, it would have been obvious at the time the invention was made to the add specific quantities of trehalose to the vaccine compositions of LaPosta et al because the addition of specific quantities of trehalose would be well within the level of skilled in the art and would be a matter of optimizing experimental parameters. Additionally, LaPosta et al teach that the addition of a sugar such as trehalose to the vaccine composition prior to freezing or lyophilization provides a composition which after freezing can be thawed to afford an aqueous colloidal suspension without further sonication of or alternatively after lyophilization can be reconstituted with a suitable aqueous diluent without further sonication (column 3, lines 10-24). It would be expected barring evidence to the contrary that vaccine comprising trehalose would retain their stability in long-term storage.

Applicant urges that the present invention is not obtained by mere optimization of experimental parameters. Applicant urges that the addition of trehalose has the surprising effect to preserve the immunogenicity of the polysaccharide-protein conjugate without the need to lyophilize or freeze it. Applicant urges that page 5 of the instant specification demonstrate that liquid compositions according to the invention maintain immunogenicity for at least 3-6 months. Applicant urges that LaPosta et al fails to provide any suggestion to combine trehalose with a polysaccharide-protein

conjugate with any expectation that the immunogenicity of the polysaccharide would be preserved as taught in the present application.

Applicant's arguments filed March 12, 2004 have been fully considered but they are not persuasive. It is the Examiner's position that Applicant is arguing limitations that are not recited in the claims. There is no limitation or requirement in the claims that the addition of trehalose would enhance immunogenicity of the polysaccharide used in the claimed method. There is no limitation in the claims that requires that the vaccine composition is not to be froze or lyophilized. LaPosta et al teach a method of stabilizing a liquid vaccine composition comprising at least one antigen consisting of a polysaccharide bound to a carrier protein, wherein it consists in adding trehalose to the vaccine composition by teaching that sugars such as trehalose may be added to the vaccine composition to prevent aggregation (i.e. stabilize) of the vaccine composition. Therefore, it is the Examiner's position that the method as taught by LaPosta et al anticipate the claimed invention.

6. The rejection of claims 1-8 and newly submitted claims 11-16 under 35

U.S.C. 103(a) is maintained for the reasons set forth on pages 6-8, paragraph 8 of the previous Office Action.

The rejection was on the grounds that Anderson et al teach vaccine comprising covalent attachment of capsular polymer fragment derived from bacterial capsular polymers to bacterial toxoids (column 2, lines 58-64). Anderson et al teach that suitable carrier proteins of the inventions include diphtheria and tetanus toxoids (columns 5, lines 29-36). Anderson et al teach that vaccine of the invention include vaccines against systemic infections caused by the pathogens *Haemophilus influenzae* type b, *E. coli*, pneumococcus, meningococcus, streptococcus and pseudomonas (column 6, lines 59-65). Anderson et al teach that the regulation of any reaction parameter, e.g. time,

Art Unit: 1645

temperature, pH, etc. which affects the reactivity or rate of reaction will alter the final composition and structure of the conjugate (column 4, lines 45-49). Anderson et al teach that the vaccines of the invention have been lyophilized (column 18, lines 35-40). Anderson et al teach that the conjugates of the invention appear to convert into macromolecular aggregates after preparation (column 13, lines 67-68 and column 14, lines 1-2).

Anderson et al do not teach the use of trehalose.

Roser et al teach the use of trehalose as a means of protecting substances such as vaccines from aggregation (see the Title and the Abstract). Roser et al teach that the addition of trehalose to biologically active substances can reduce aggregation during dehydration and rehydration (page 4). Roser et al teach that the addition of trehalose prevents the formation of all multimeric forms of the substance (page 5). Roser et al teach the addition of trehalose in the amount of about 1% to 50% more preferably about 5% to 25% to biologically active substances (page 7). Roser et al teach that material dried in the presence of trehalose, when resuspended produces a smooth and single particulate suspension (page 9).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the trehalose as taught by Roser et al to the immunogenic conjugate vaccines of Anderson et al because Roser et al teach the use of trehalose as a means of protecting substances such as vaccines from aggregation and Roser et al also teach that the addition of trehalose prevents the formation of all multimeric forms of the substance. It would be expected barring evidence to the contrary that vaccine comprising trehalose would retain their stability in long-term storage.

Applicant urges that Anderson et al in view of Roser et al fail to render claims 1-8 obvious in view of the surprising result that the addition of trehalose to a polysaccharide-protein conjugate preserves the immunogenicity of the conjugate.

Applicant's arguments filed March 12, 2004 have been fully considered but they are not persuasive. It is the Examiner's position that Applicant is arguing limitations that are not recited in the claims. There is no limitation or requirement in the claims that the addition of trehalose would enhance immunogenicity of the polysaccharide used in the claimed invention. Anderson et al teach that vaccine of the invention include vaccines against systemic infections caused by the pathogens *Haemophilus influenzae* type b, *E.*

Art Unit: 1645

*coli*, pneumococcus, meningococcus, streptococcus and pseudomonas that can be conjugated to carrier such as diphtheria and tetanus toxoids. Anderson et al do not teach the use of trehalose. However, Roser et al teach that the addition of trehalose to biologically active substances can reduce aggregation during dehydration and rehydration (page 4). Therefore, it would be obvious to add the trehalose as taught by Roser et al to the immunogenic conjugate vaccines of Anderson et al because Roser et al teach the use of trehalose as a means of protecting substances such as vaccines from aggregation and Roser et al also teach that the addition of trehalose prevents the formation of all multimeric forms of the substance. There is nothing on the record to show that the combination of teachings would not suggest the claimed invention.

### ***Status of Claims***

7. No claims allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of



Art Unit: 1645


the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.


10. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov/>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
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May 25, 2004

  
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